

Effects of the pathological characteristics on the presence of multicentric thyroid tumors in the contralateral lobe

Multicentric papillary thyroid carcinoma

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Abstract

Aim: In this study, we aimed to investigate the effects of pathological tumor characteristics on the presence of a multicentric tumor in the contralateral lobe in papillary thyroid carcinoma (PTC).

Material and Methods: A total of 46 patients aged over 18 years who underwent total thyroidectomy due to PTC in our clinic were retrospectively evaluated. Patients' demographic data such as age and gender, preoperative USG findings, postoperative pathological findings, lobe localization, and the presence of nodules in the contralateral lobe were recorded. In addition, tumor size, presence of nuclear atypia, mitotic activity, vascular invasion and extrathyroidal spread of the tumor and the presence of lymph node metastasis were obtained from pathological reports. Patients were divided into two groups as multicentric and non-multicentric, and the data were compared between these groups.

Results: The mean age of the patients was 44.9 ± 12.3 years. Twenty-three patients had papillary thyroid microcarcinoma and 23 patients had papillary thyroid carcinoma. Postoperative pathological examination revealed multicentric PTCs in 15 patients. No statistically significant difference was found between patients with and without multicentric contralateral lobe tumors in terms of primary tumor diameter, nuclear atypia, mitotic activity, tumor necrosis, vascular invasion, extrathyroidal spread and lymph node metastasis (for all $p > 0.05$).

Discussion: The pathology of the tumor in the contralateral lobe of the primary nodule can be seen with preoperative USG in the majority of patients with PTC. The presence of a multicentric tumor in the contralateral lobe is not correlated with tumor size and pathological characteristics of the tumor.

Keywords

Papillary Thyroid Carcinoma, Microcarcinoma, Multifocal, Multicentric, Tumor Size, Metastasis

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Introduction

Papillary thyroid cancer (PTC) is the most common (85%) histological subtype of thyroid carcinomas with an increasing incidence [1]. PTC rarely shows aggressive behavior and usually has a good prognosis; however, it should be evaluated carefully due to the potential for distant metastasis [2]. Total thyroidectomy followed, in appropriately selected cases, by radioiodine ablation is a well-established surgical treatment option for the management of PTC [3]. This approach has several advantages: complete removal of the thyroid gland allows detection and ablation of metastatic disease and eliminates the possibility of residual carcinoma undergoing anaplastic transformation [4]. Although PTC often has an insidious course, tumors with some clinicopathological features may exhibit a more aggressive course. Among these, multifocality is often considered a high-risk factor for progression of PTC, prompting more aggressive treatments [5]. Multifocality is defined as the presence of PTCs in two or more foci. Multifocal PTC may present as microcarcinoma or larger lesions in two or more locations within the thyroid gland. Studies have shown that multifocality mostly involves the dominant nodule and surrounding microcarcinomas by approximately 90% [6, 7]. Multifocality occurs in 20-30% of PTC cases, but this rate is highly variable depending on the methodology used and the extent of the histopathological sampling, and the incidence of multifocal PTC is reported to increase [8]. On the other hand, multifocality may lead to undertreatment or overtreatment, depending on how a clinician uses it as a prognostic factor [5]. Arising of thyroid nodules independently in the contralateral lobe is defined as multicentricity. Multicentric occurrence of PTCs may be common, possibly higher than 30%. The exact mechanisms underlying multicentric PTCs are yet to be fully understood. Bilateral thyroid nodules are commonly detected by ultrasonography (US) in patients with pathologically confirmed PTC in one lobe [9]. The incidence of contralateral lobe nodules has been reported as high as 48% in patients diagnosed with unilateral PTC [10]. According to the 2015 American Thyroid Association (ATA) guidelines, the presence of contralateral lobe thyroid nodules may be considered criteria for recommending total or completion thyroidectomy [11]. The prognostic value of multifocality/multicentricity remains controversial, leading to a major challenge in the clinical management of PTC [5]. Some retrospective studies have reported a correlation between multifocality/multicentricity and the prognosis of PTC, while others reported no difference between multifocal and unifocal disease [12, 13]. There are insufficient literature studies investigating multicentric contralateral thyroid lobe carcinomas. Therefore, in this study, we aimed to investigate the effects of pathological tumor characteristics on the presence of multicentric tumor in the contralateral lobe in papillary thyroid carcinoma.

Material and Methods

Before the study began, the study protocol was approved by the local ethics committee with the 11.11.2021 dated and 2/2021.K-81 numbered decision. The study was conducted in accordance with the Declaration of Helsinki (as revised in

2013). Patient consent was waived as the study was conducted retrospectively. Patients aged over 18 years, who underwent total thyroidectomy duo to PTC in our clinic between 2016 and 2020 were retrospectively evaluated. Patients under 18 years old, those with recurrent carcinomas, non-papillary histology, distant metastasis at presentation, patients who underwent subtotal thyroidectomy and those with missing preoperative and postoperative data were excluded from the study. Patients' demographic data such as age and gender, preoperative USG findings, postoperative pathological findings, lobe localization and the presence of nodules in the contralateral lobe were recorded. In addition, tumor size, presence of nuclear atypia, mitotic activity, vascular invasion and extrathyroidal spread of the tumor, and the presence of lymph node metastasis were obtained from the pathological reports. The lobe with the nodule of larger diameter was considered a tumor lobe. Patients with cancerous nodules in the contralateral lobe were considered to have multicentric carcinoma. Multicentric characteristic of the tumors was confirmed with postoperative pathological examination. Patients were divided into two groups as multicentric and non-multicentric, and the data obtained were compared between the two groups.

Statistical Analysis

Statistical analysis of the data obtained in this study was performed using SPSS version 20.0 (SPSS, Statistical Package for Social Sciences, IBM Inc., Chicago, IL, USA) statistical software. Continuous variables were expressed as mean±standard deviation, and categorical variables as frequency (n) and percentage (%). The independent t-test was used to compare variables between the groups. The p values <0.05 were considered statistically significant.

Results

The study included 46 patients, aged between 20-76 years,

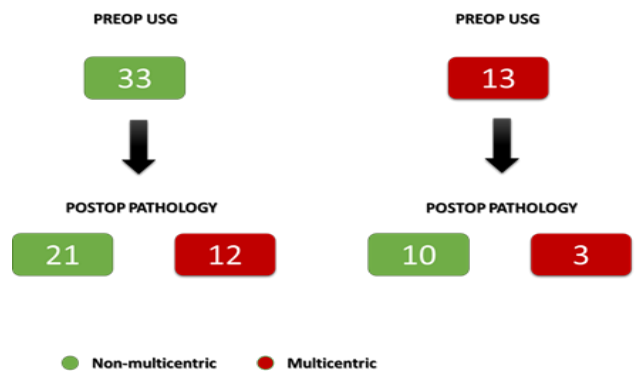


Figure 1. Multicentric / Non-multicentric distribution of the PTCs

Table 1. Carcinoma and microcarcinoma distributions of all tumors

	Total		Microcarcinoma		Carcinoma	
	n	%	n	%	n	%
Multicentric	15	32.6	8	17.4	7	15.2
Non-multicentric	31	67.4	15	32.6	16	34.8
Total	46	100.0	23	50.0	23	50.0

who underwent total thyroidectomy due to PTC in our clinic during the study period. Of all patients, 29 (63.0%) were female and 17 (37.0%) were male. The mean age of the patients was 44.9 ± 12.3 years. Twenty-three (50.0%) patients had papillary thyroid microcarcinoma and 23 (50.0%) patients had papillary thyroid carcinoma. Tumor localization was found as the right lobe in 23 (50.0%) and the left lobe in 23 (50.0%) patients. The mean tumor diameter was measured as 14.0 ± 10.7 (range: 3-45) mm.

The patients were divided into two groups, based on the presence of contralateral lobe tumors, as multicentric and non-multicentric. In the preoperative USG examination, 33 (71.7%) patients had contralateral lobe nodules, while 13 (28.3%) patients had no contralateral lobe nodules. Ten (76.9%) of the 13 non-multicentric patients had no carcinoma in both preoperative USG examination and postoperative pathological evaluation. In the remaining three (23.1%) patients, while no nodule was detected on postoperative USG examination, postoperative pathological outcome was reported as contralateral lobe tumor. All of these patients had microcarcinomas.

In the multicentric group (n=33), postoperative pathological outcomes were reported as contralateral lobe tumors (multicentric) in 12 (36.4%) patients. Therefore, a total of 15 patients (3+12) were considered to have multicentric PTCs. The distribution of the PTCs according to the preoperative USG and postoperative pathological findings is shown in Figure 1. Carcinoma and microcarcinoma distributions of the PTCs are given in Table 1.

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Pathological reports of the multicentric and non-multicentric groups were compared. Accordingly, no correlation was found between carcinoma/microcarcinoma distinction and the presence of contralateral lobe tumors ($p=0.099$). No statistically significant difference was found between the patients with multicentric and non-multicentric tumors in terms of the primary tumor diameter ($p=0.077$). In addition, no statistically significant difference was found between the patients with and without contralateral lobe tumors in terms of nuclear atypia ($p=0.12$), mitotic activity ($p=0.076$), tumor necrosis ($p=0.15$), vascular invasion ($p=0.67$), extrathyroidal spread ($p=0.99$) and lymph node metastasis ($p=0.35$).

Discussion

In this study, we investigated the effects of several tumor characteristics on the presence of contralateral lobe tumors, namely multicentricity. Multicentricity in PTC is not defined as a factor affecting prognosis in guidelines. However, studies have associated multicentric PTC's with increased recurrence rates, lymph node involvement, distant metastasis and mortality [14]. The rate of multicentric PTCs has been reported between 18%-87% in the literature [15]. In the present study, the rate of multicentric PTCs was found as 28.3% with preoperative USG and 32.6% according to the postoperative pathological

examination. In a study by Zhang et al. including 221 patients with PTC, the rate of multicentric tumors was 21.7% [8]. In a study by Iscan et al., the rate of multicentricity was found as 23% in PTCs < 5 mm [16]. The rate of multicentric tumors found in our study was consistent with the rates reported in previous studies.

Although not fully understood, the pathogenesis of multilocal PTCs can be explained by both multicentric occurrence and intrathyroidal metastasis. However, there is still controversy in the explanation of multifocality. It is important to clarify this issue in order to guide treatment decisions and to determine prognosis in patients with PTCs [17]. Multifocal PTC is usually defined as small foci surrounding the primary tumor. There is no consensus in the literature on the effect of multifocal PTC on prognosis in terms of recurrence [12]. To our knowledge, there is no study evaluating the multicentric cancer focus seen only in the contralateral lobe of the thyroid lobe where the primary nodule is located, which may explain the lack of consensus on prognosis in the literature on multifocal PTC. Since the disease in the same lobe can be eliminated with partial surgery such as lobectomy, any millimetric focus that cannot be seen with preoperative USG in the contralateral lobe can cause a recurrence. We did not evaluate recurrence in our patients; however, we performed total thyroidectomy in all patients. The effect of any nodule in the lobe on revision surgery over time can be evaluated with further studies by following the contralateral lobe in patients who underwent partial thyroidectomy.

PCT prognosis has been shown to be associated with several factors including tumor size, vascular invasion, extrathyroidal spread, and the presence of lymph node metastasis. However, on the contrary, there are studies that could not find such associations [18, 19]. We found that the presence of multicentric PTC in the contralateral lobe was not correlated with pathological characteristics such as nuclear atypia and mitotic activity of the primary tumor, necrosis and vascular invasion. In addition, the presence of multicentric PTC in the contralateral lobe was not associated with extrathyroidal spread and lymph node metastasis. Perhaps if we had evaluated multifocality for more than one tumor in the same lobe, we would have obtained different data. However, we evaluated the individual tumor in the contralateral lobe, and the data we obtained showed that both tumors did not have interrelated effects.

In the present study, we demonstrated that the majority (13/15, 87%) of the contralateral lobe PCTs can be detected through preoperative USG examination, and the remaining tumors that could not be detected with preoperative USG were microcarcinomas. Papillary microcarcinomas < 10 mm can also be detected by USG. However, it is very difficult to detect patients with a tumor size ≤ 3 mm using USG [20]. In our study, 3 of 13 patients without nodules detected by preoperative USG had papillary microcarcinoma in the pathological reports.

We think that this should be taken into account in preoperative patient evaluations. Tumor size ≥ 20 mm in PTC affects pathological features such as lymph node metastasis and extrathyroidal spread, making the tumor more aggressive [21]. In a study by Lin et al., the mean size of the dominant focus was shown to be significantly smaller in a multicentric tumor compared to the unifocal tumor [22]. On the contrary, in a study

by Hwang et al., no correlation was found between the tumor size and multicentricity [23]. Similarly, in the present study, no significant correlation was found between the presence of a multicentric tumor in the collateral lobe and the size of the primary tumor. This may be related to the fact that the mean tumor size of the patients in our study was < 20 mm.

Study Limitations

The major limitations of this study are its retrospective nature and a relatively small number of patients. In addition, tumor sizes could be classified and multifocal/multicentric tumor distinction could be made considering the invasion in relation with the primary tumor.

Conclusion:

The pathology of the tumor in the contralateral lobe of the primary nodule can be seen with preoperative USG in the majority of patients with PTC. It should be remembered that there may be microcarcinoma foci in patients without pathology detected by USG. In addition, the presence of a multicentric tumor in the contralateral lobe is not correlated with tumor size and pathological characteristics of the tumor.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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